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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,379	05/30/2001	Donald L. Durden	1857-P02575US1	7235

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EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 09/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/870,379	DURDEN, DONALD L.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-80 and 82-90* is/are pending in the application.

4a) Of the above claim(s) *1-79 and 83-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80, 82, 89, and 90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

This application contains claims 1-79, and 84-88 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-79, and 84-88 remain withdrawn for reason of record from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 1-80, and 82-90 are pending and claims 80, 82, 89, and 90 are examined on merits.

Claim Rejections - 35 USC § 112

Claims 80, 82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant argues that assay to screen the compounds with the function is known iand two compounds that belong to the genus is known but this argument is not persuasive because the two art-known compounds do not share common structures for the same function. It is concluded that applicant did not posses the claimed genus other than LY294002 and wortmannin. LY294002 and

wortmannin do not share common structures although they have same function. Although it is possible to screen compounds with the function, the written description rejection is still maintained because the specification does not disclose the common chemical structures necessary for the function.

Claim 82 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant argues on two points. First, applicant argues "PI3 kinase inhibitor" and "an AKT inhibitor" are same because PI3 and AKT are in same signaling pathway. This argument is not persuasive because the specification as originally filed does not convey that they are the same, see for example see pages 1-5, where it suggests that "an AKT inhibitor" and "PI3 kinase inhibitor" are different entities and can be screened with the assay disclosed in the instant application: it does not make any sense to give two different names for a single entity. Further, the art recognizes LY294002, see for example, Li et al (IDS C1), as PI3 kinase inhibitor, not "an AKT inhibitor" although the art already knows PETN regulates AKT/PI3 signaling pathway. Zhou et al (the abstract applicant attached to show that ATK inhibitor is known in the art) says that something inhibits ATK does not necessarily inhibit PI3, so they could not be the same. It is concluded that C2-ceramide is only known ATK inhibitor in the art.

Claim 82 remain rejected for reason of record under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to **enable** one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant argues that the art discloses C2-ceramide as an ATK inhibitor and the specification discloses the animal model for assaying various activities. However, this argument is not persuasive because the claim is drawn to in vivo method of inhibiting angiogenesis. The specification does not teach that C2-ceramide or any other ATK inhibitor could accomplish the purpose set out in the preamble of the claim. Since it experiment involves in vivo experiments with its outcome unpredictable as explained in the previous Office action, the specification provides insufficient guidance whether C2-ceramide could inhibit in vivo angiogenesis, does not teach how to make any other ATK inhibitor capable of accomplishing the purpose stated in the preamble, and provides no working, it is concluded that undue experimentation would be required to practice the claimed invention.

Response to Amendment

The Declaration of Dr. Durden filed on 6-19-2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the Hu et al reference.

The 1.131 declaration is intended to show prior conception of the invention and due diligence in reduction to practice. Exhibit A is cited as evidence of conception. Exhibit A refers to introducing genes into human brain tumor cells, specifically that transferring a gene (PTEN) into brain tumor cells prevents growth of the tumor. This

exhibit does not in any way demonstrate conception of the claimed invention of "administration of a PI-3 kinase inhibitor" to "a patient in need" of "inhibiting aberrant tumor-induced angiogenesis." Since the evidence is insufficient to establish conception prior to the reference date, the evidence regarding due diligence is moot

Claim Rejections - 35 USC § 102

Claim 80 remains rejected and the new claims 89 is also rejected for reason of record under 35 U.S.C. 102(a) as being anticipated by Hu et al (March 2000, Clinical Cancer Research, vol. 6, pages 880-886) as evidenced by Jiang et al (02-15-2000, PNAS vol. 97, pages 1749-1753) and Oikawa et al (1996, European Journal of Pharmacology, vol. 318, pages 93-96).

Applicant argues Hu et al do not teach instant invention because administering a PI3 inhibitor to tumor-bearing mice by Hu et al caused apoptosis, not inhibiting angiogenesis. But this argument is not persuasive because endothelial apoptosis is same as inhibiting angiogensis since apoptosis of endothelial cells involved would lead inhibition of angiogenesis according to Shibuya, Cancer Sci. 2003 Sep;94(9):751-6.

Since the declaration is defective as explained above, Hu et al is still a prior art.

NEW GROUNDS OF REJECTION

Claim Objections

If applicant could overcome the written description rejection of claim 82 above, then claim 82 is objected and rejected as follows:

This rejection is based on applicant's argument at page 5, 1st paragraph in Paper No. 10 that "an AKT inhibitor" and "a PI3 kinase inhibitor" are same.

Claim 82 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant states on the record in the amendment (Paper No. 8), the limitation "an AKT inhibitor" in the claim is same as "PI3 kinas" of claim 80. This statement indicates that although different words are used in claim 82, claim 82 does not further limits the base claim.

Claim Rejections - 35 USC § 112

If applicant could overcome the written description rejection of claim 82 above, then claim 82 is objected and rejected as follows:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 80, and 82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is based on applicant's argument at page 5, 1st paragraph in Paper No. 10 that "an AKT inhibitor" and "a PI3 kinase inhibitor" are same thing. The Office is completely confused why the claims have two different limitations to mean same thing.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 90 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al as applied to claim 80 above, and further in view of Oikawa et al (a copy provided in the previous Office action, 1996, European Journal of Pharmacology, vol. 318, pages 93-96).

The claim is drawn to method of inhibiting tumor-induced angiogenesis in vivo by administering the fungal metabolite, wortmannin. The primary reference teaches all the necessary steps and reagents for in vivo treatment and Oikawa et al teach wortmannin is well known in the art and inhibits angiogenesis. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use wortmannin inhibits angiogenesis induced by cancer with a reasonable expectation of success. Note the last line of the abstract by Oikawa et al.

Double Patenting

If applicant could overcome the written description rejection of claim 82 above, then claim 82 is objected and rejected as follows:

This rejection is based on applicant's argument at page 5, 1st paragraph in Paper No. 10 that "an AKT inhibitor" and "a PI3 kinase inhibitor" are same thing.

Claim 82 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 80. Applicant argues, in response to written description rejection of the limitation "an AKT inhibitor" in instant claim 82, that "an AKT inhibitor" is same as "a PI3 kinase inhibitor. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is

proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
September 13, 2003

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1600